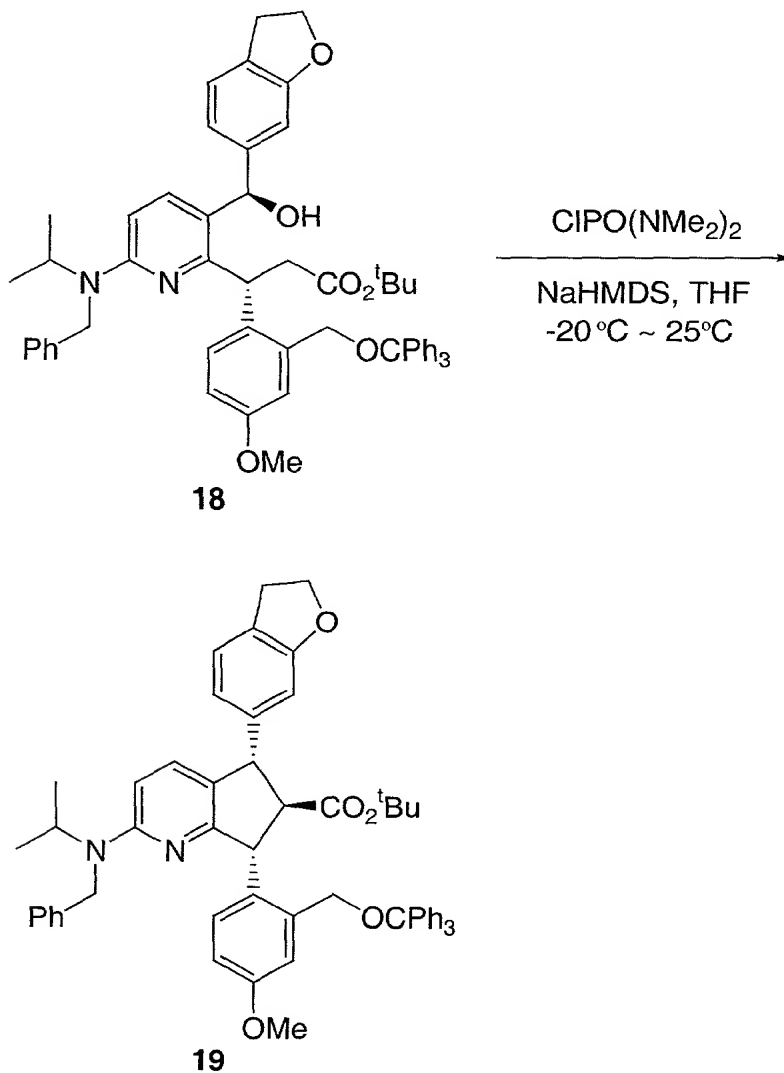


Normal phase HPLC conditions for diastereoselectivity measurement: YMC PVA 4.6 x 250mm; hexane:IPAc (95:5); 1.00mL/min; UV detection at 220nm; Retention times (min): major isomer (9.1) and minor isomer (7.4).

EXAMPLE 11

5 Cyclization:

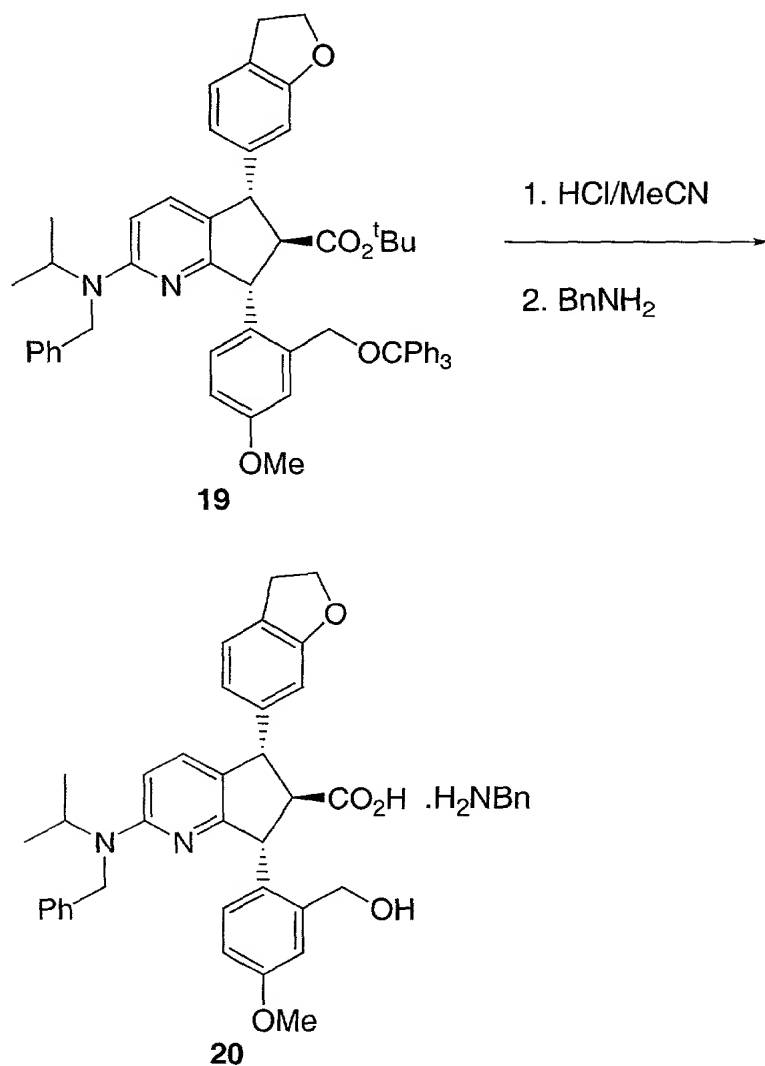


To a 5L four-neck round-bottom flask equipped with a dropping funnel, a mechanical stirrer, a thermocouple thermometer and a nitrogen inlet is added the crude Grignard addition product **18** (780g, 295g assay) and THF (1.2L). The

system is degassed by vacuum/N₂ cycle and then cooled to -20°C. CIP(O)(NMe₂)₂ (74mL, 0.5mol, 1.5 equiv.) is added followed by slow addition of NaHMDS (1.67L, 2 hours) at about -20°C to 0°C by a dropping funnel. The mixture is then aged for 3 hours at 0°C and the completion of the reaction was confirmed by HPLC (<1A% SM).

- 5 Additional amount of CIP(O)(NMe₂)₂ (0.1 equiv.) and NaHMDS (0.2 equiv.) may be added if necessary. The reaction is quenched by slowly adding about 600mL of water followed by slow addition of 400mL of acetic acid. The mixture is stirred for about 0.5 hour at 15°C to 25°C, and then the layers are separated. The organic layer is washed with 1.0L of (1:1) brine:water and then 1.0L of brine. It is concentrated under
- 10 reduced pressure (30~60mmHg, 40°C bath) to 666g and then flushed with 660mL of MeCN (90~40mmHg, 40°C bath). The crude product **19** is used directly for the deprotection step.

EXAMPLE 12

Deprotection and Benzylamine Salt Formation:

To a 5L three-neck round-bottom flask equipped with a mechanical stirrer, a thermocouple thermometer and a dropping funnel is charged with about 2L of MeCN. The mixture is cooled to 0°C and then 900mL of concentrated HCl is added by a dropping funnel at <15°C. The crude cyclization product (625g crude, about 250g pure) is diluted with 400mL of MeCN and then charged into the HCl in MeCN solution at 5°C to 15°C. The starting material flask is rinsed with additional amount of acetonitrile. The mixture is allowed to warm to 20°C and stirred overnight.